REMARKS

Status of the Claims

Claims 23, 28-30, 36 and 50-80 are pending.

Claims 23, 28-30, 36 and 50-80 were rejected.

By way of this amendment, new claims 81-89 have been added.

Upon entry of this amendment, claims 23, 28-30, 36 and 50-89 will be pending.

Summary Amendment

New claims 80-89 refer to specific embodiments of the invention. Support for new claims 80-89 is found throughout the specification and claims as originally filed. No new matter has been added.

New claims 80-89 each correspond to and cover the elected invention and species.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 23, 28-30, 36 and 50-80 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way to enable one of ordinary skill in the art, to which it pertains or to which it is most nearly connected, to make and/or use the invention.

The position of the Office that there are problems associated with the use of antibodies to treat cancer and that such therapies are unpredictable. The Office has cited references by Weiner, Jain and Dillman in support of the rejection.

In earlier responses, Applicant has pointed out that each of the references cited in support of the rejection actually support a conclusion that the invention is enabled. Applicant respectfully urges that the Office is misapplying the standard for enablement. The scientific and clinical analysis apply different standards than those required for patentability when evaluating technology and its use in the treatment of diseases.

Similarly, a product need not be commercially viable to meet the requirements under the first paragraph of 35 U.S.C. §112.

It is well settled that the Office has the initial burden of establishing that a claimed invention does not meet the enablement requirement and only upon meeting its burden does the burden shift to the Applicant. The Office has failed to meet its burden. While the Examiner has set forth evidence, the evidence in fact supports a finding of enablement. The Office has not established that the claimed invention does not meet the enablement requirement. Failing to do so, the burden is not properly shifted to the Applicant.

Applicant respectfully urges that one skilled in the art would accept Applicants' assertion of enablement. Applicant respectfully urges those skilled in the art would accept that the claimed invention is operable despite references in the past which describe the various technical issues which arise in developing an antibody therapeutic.

As pointed out earlier, while Jain and Dillman were cited as pointing out problems and obstacles in developing antibody based therapeutics, both references also discuss the promise of antibody-based therapeutic. Further, as Applicant urged earlier, Weiner dispels any doubts suggested by Jain or Dillman and puts in proper context the issues raised in those references. Weiner provides strong evidence that those having ordinary skill in the art would accept Applicant's assertion of enablement. Weiner provides strong evidence supporting Applicant's position. As noted earlier, Weiner's abstract states:

> Monoclonal antibody-based therapeutics are beginning to realize the promise that was predicted with the advent of the core technology more than 20 years ago.

Weiner states in the last sentence of the full paragraph on the right column of page 41 that prior evaluations reached

> the premature and unwarranted conclusion that antibody-based therapeutics do not show sufficient promise to be considered cutting-edge and valuable

In the first complete sentence on page 42, Weiner states that

> [e]ncouraging clinical results will be described in which antibodies are used to... .... (4) deliver radionuclides, toxins and chemotherapeutic agents.

On page 43, in the first paragraph of the section entitled "Factors regulating antibody based tumor targeting" Weiner states that

> [i]t should be emphasized that the identification of obstacles is not a reason for discouragement

indicating that they are merely part of the development process

Weiner provides evidence that those skill in the art would believe the objective truth of Applicant's assertion that the claimed invention is enabled. Weiner also discusses on page 48 drug immuno-conjugates, such as those used in the claimed invention, as an improvement over conventional chemotherapy. The summary on page 49 refers to the development of clinical uses of antibodies offers and the promise and expectations that those of having ordinary skill in the art have.

It has not been contradicted that the Weiner reference, cited by the Examiner in the first Office Action (Seminars Oncology (1999) 26:41-50), despite pointing out several obstacles to be overcome in order to maximize clinical effectiveness of antibody therapy in cancer treatment, clearly indicated that the presence of these obstacles is "not a reason for discouragement", and that "properly exploited, the [binding to tumor antigens] of MoAb and the their derivatives led to some striking examples of antitumor effects". These statements do not support a finding of non-enablement but rather are consistent with Applicant's assertion. Regarding drug immunoconjugates, and radioimmunoconjugates, Weiner states that, "early studies of RIT have shown that partial short-lived clinical responses can be achieved in some patients with advanced solid tumors", and concludes with statements that overall results are "promising" and "are expected to add to the list of novel agents available for the treatment of malignancies....". These statements do not support a finding of non-enablement but rather are consistent with Applicant's assertion. The criteria for enablement is not the achievement of perfect

therapeutic indicia free of side effects and complications. Weiner illustrate that treatments with the antibodies of the invention would be predictively operative to a degree that can be measured in clinical studies. And this is the test for an adequate disclosure of how to make and use the claimed invention.

As noted earlier, the Dillman reference was published before the application was filed. The abstract refers to *"limited clinical efficiency"*. It is well settled that limited clinical efficacy is sufficient to establish compliance with the enablement requirement of the patent law. As noted earlier, Dillman noted that *"trials of antibody alone and radiolabeled antibodies have confirmed the feasibility of this approach...."* These statements do not support a finding of non-enablement but rather are consistent with Applicant's assertion. According to Dillman the technique of antibody therapy shows that the cancer immunotherapy community as of 1989 believed that antibody therapy was "feasible and promising" as a therapeutic modality.

The Court of Appeals for the Federal Circuit in Chiron Corp. v. Genentech, Inc., 363 F.3d 1247 (Fed. Cir. 2004), acknowledged that murine antibodies are useful for short-term therapies and can only be used in long-term therapies with a significant risk of a deleterious immunogenic response. The short term use of murine antibodies is sufficient to establish enable under the patent law. The standards used by the Office are different from those used by the FDA in making marketing approval decisions or those used by companies deciding to commercially develop drugs.

The claimed invention is enabled. The evidence relied upon by the Office in support of the rejection does not in fact support the conclusion that one skilled in the art would doubt the object truth of Applicant's assertion of enablement. When all of the evidence is viewed in its totality one skilled in the art would accept the object truth of Applicant's assertion of enablement. The evidence of record supports a finding that the invention is enabled as required under the law. Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Non-statutory Double Patenting

Claims 23, 28-30, 36 and 50-57 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over 1, 5, 9-10, 30, 31, 55, 56 and 58 of U.S. Patent No. 5,879,656. As noted earlier, once claims have been indicated to be allowable, Applicants shall promptly provide Terminal Disclaimer as appropriate. To that end, the Examiner is invited to contact Applicants' undersigned representative and inform him of the allowability of the claims so that a Terminal Disclaimer can be promptly filed by telefax.

Conclusion

For the foregoing reasons, claims 23, 27, 28-30, 36 and 50-89 are in condition for allowance. Applicants invite the Examiner to contact the undersigned at 215.665.5592 to clarify any unresolved issues raised by this Amendment. A notice of allowance is earnestly solicited.

As indicated on the transmittal accompanying this response, the Commissioner is hereby authorized to charge any debit or credit any overpayment to Deposit Account No. 50-1275.

Respectfully submitted,

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Dated: August 23, 2006
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